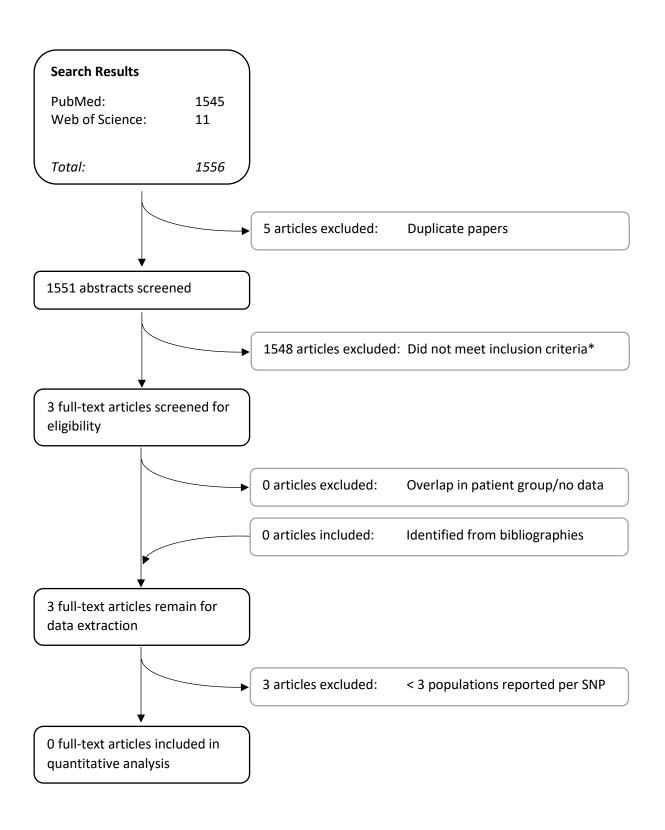
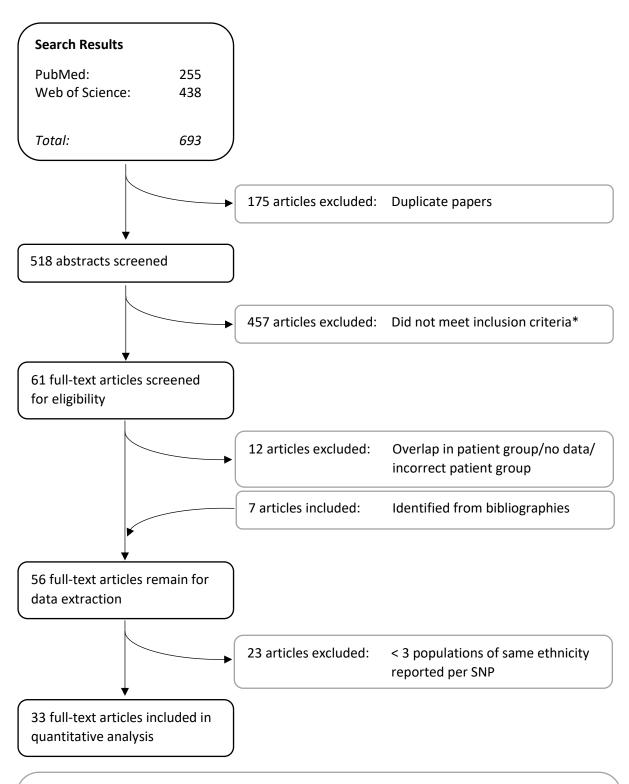


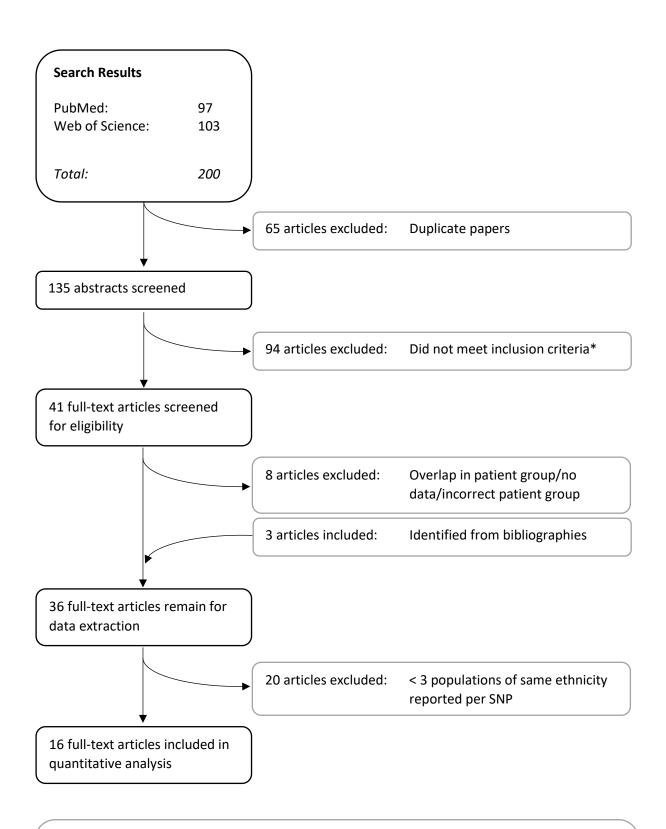
\*Inclusion criteria: Any paper was removed from the analysis if it was not written in English or Spanish (n=20), was a non-human study (n=5), was a paediatric study (n=52), was not a case-control study (n=36), did not have a renal disease phenotype (n=90), did not include data for *ACE* (n=13) or had a pharmaceutical drug focus (n=9)



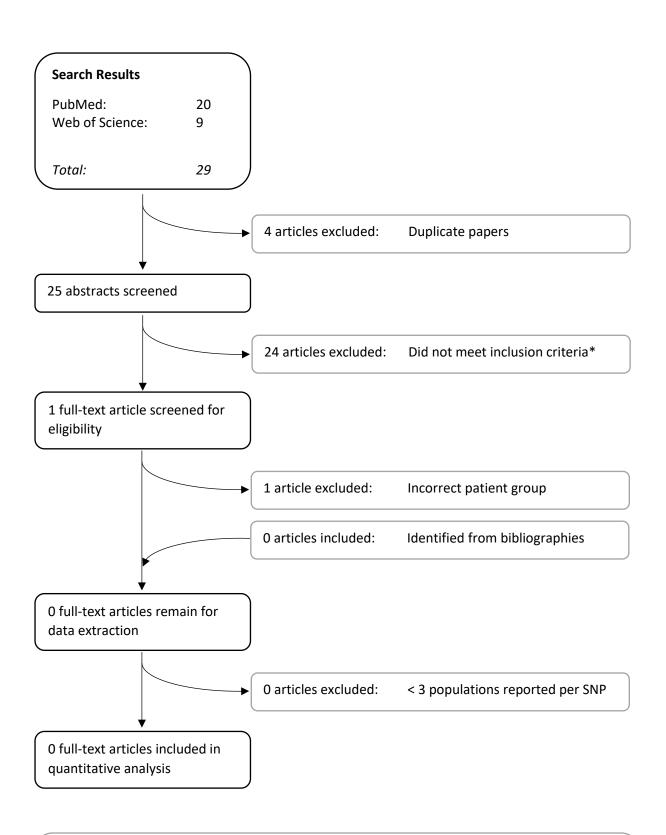
\*Inclusion criteria: Any paper was removed from the analysis if it was not written in English or Spanish (n=55), was a non-human study (n=119), was a paediatric study (n=149), was not a case-control study (n=53), did not have a renal disease phenotype (n=693), did not include data for ACE2 (n=435) or had a pharmaceutical drug focus (n=44)



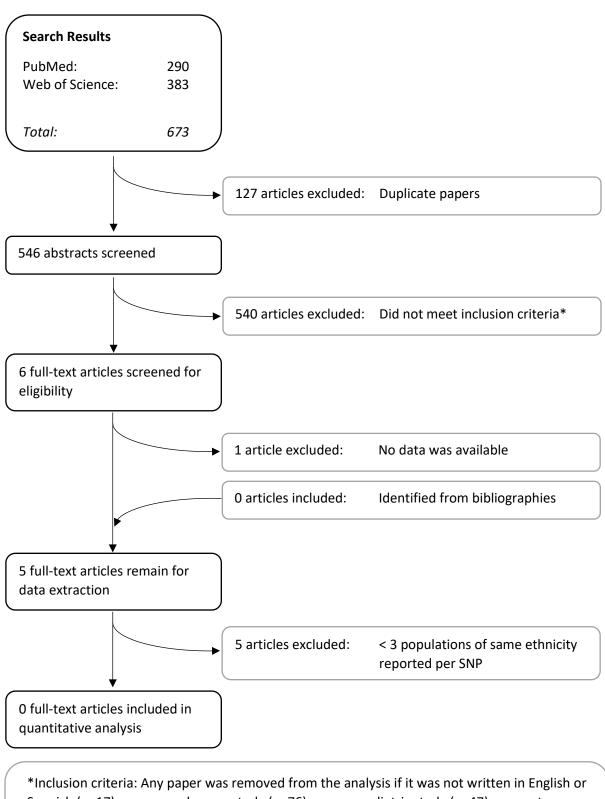
\*Inclusion criteria: Any paper was removed from the analysis if it was not written in English or Spanish (n=16), was a non-human study (n=121), was a paediatric study (n=40), was not a case-control study (n=54), did not have a renal disease phenotype (n=134), did not include data for AGT (n=75), was a gene expression based study (n=1) or had a pharmaceutical drug focus (n=16)



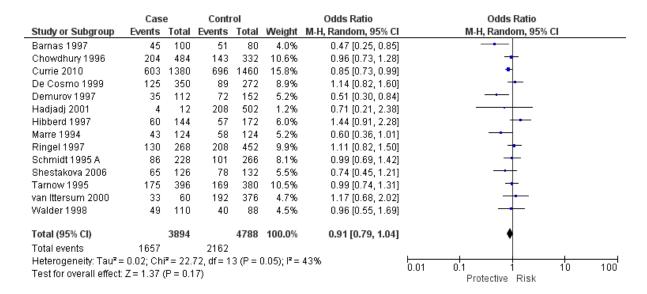
\*Inclusion criteria: Any paper was removed from the analysis if it was not written in English or Spanish (n=8), was a non-human study (n=13), was a paediatric study (n=21), was not a case-control study (n=14), did not have a renal disease phenotype (n=25), did not include data for *AGTR1* (n=3), was a gene expression based study (n=1) or had a pharmaceutical drug focus (n=9)



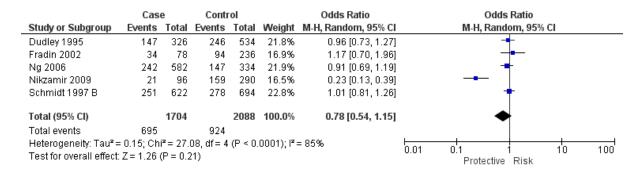
\*Inclusion criteria: Any paper was removed from the analysis if it was not written in English or Spanish (n=1), was a non-human study (n=2), was a paediatric study (n=6), was not a case-control study (n=4), did not have a renal disease phenotype (n=5) or did not include data for AGTR2 (n=6)



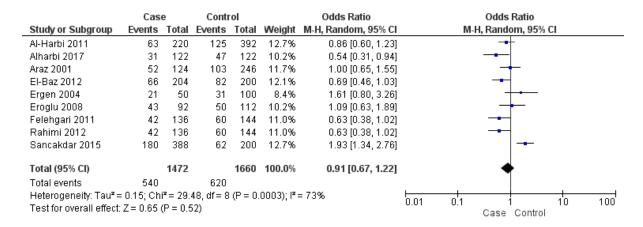
\*Inclusion criteria: Any paper was removed from the analysis if it was not written in English or Spanish (n=17), was a non-human study (n=76), was a paediatric study (n=47), was not a case-control study (n=71), did not have a renal disease phenotype (n=175), did not include data for *REN* (n=137), was a gene expression based study (n=3) or had a pharmaceutical drug focus (n=14)



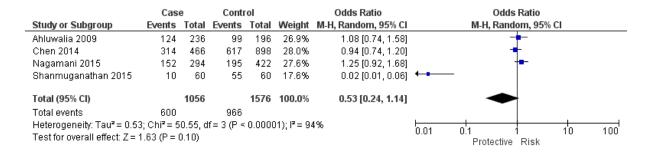
**Supplementary Figure S2a:** Forest plot - *ACE* I/D investigation, individuals with type 1 diabetic nephropathy compared to individuals with type 1 diabetes mellitus in a European population (*ACE* insertion compared to deletion).



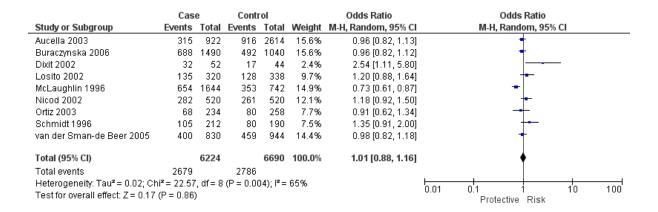
**Supplementary Figure S2b:** Forest plot - *ACE* I/D investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a European population (*ACE* insertion compared to deletion).



**Supplementary Figure S2c:** Forest plot - *ACE* I/D investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a Middle Eastern population (*ACE* insertion compared to deletion).



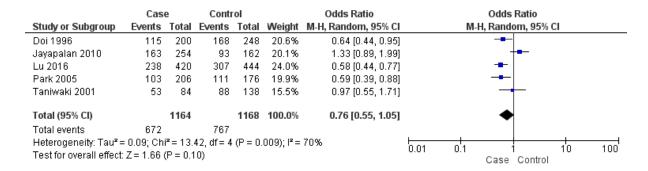
**Supplementary Figure S2d:** Forest plot - *ACE* I/D investigation, individuals with chronic kidney disease compared to healthy controls in a South Asian population (*ACE* insertion compared to deletion).



**Supplementary Figure S2e:** Forest plot - *ACE* I/D investigation, individuals with end-stage renal disease compared to healthy controls in a European population (*ACE* insertion compared to deletion).

	Protective		Protective Risk			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Abuaisha 2018	37	172	50	200	34.8%	0.82 [0.51, 1.33]	-
Rahimi 2017	64	190	89	234	50.9%	0.83 [0.55, 1.23]	<del></del>
Zaare Nahandi 2017	23	60	21	54	14.3%	0.98 [0.46, 2.08]	_
Total (95% CI)		422		488	100.0%	0.85 [0.64, 1.13]	•
Total events	124		160				
Heterogeneity: Tau² = 0	0.00; Chi²	= 0.16,	df = 2 (P	= 0.92	); l² = 0%		0.01 0.1 1 10 100
Test for overall effect: Z	:= 1.15 (P	= 0.25	)				Protective Risk

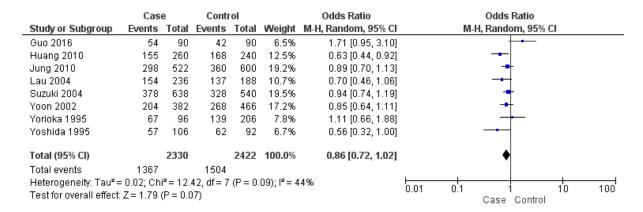
**Supplementary Figure S2f:** Forest plot - *ACE* I/D investigation, individuals with end-stage renal disease compared to healthy controls in a Middle Eastern population (*ACE* insertion compared to deletion).



**Supplementary Figure S2g:** Forest plot - *ACE* I/D investigation, individuals with end-stage renal disease linked to type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in an East Asian population (*ACE* insertion compared to deletion).

	Case		Case Control			Odds Ratio		Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% CI	
Grzeszczak 1998	128	254	244	508	33.9%	1.10 [0.81, 1.49]		<del>-</del>	
Ringel 1997	150	322	141	280	33.7%	0.86 [0.62, 1.18]		<del>-= </del>	
Schmidt 1997 A	29	122	416	694	32.4%	0.21 [0.13, 0.32]		-	
Total (95% CI)		698		1482	100.0%	0.59 [0.24, 1.44]		•	
Total events	307		801						
Heterogeneity: Tau² =	0.58; Ch	i²= 38.	0.01 0	1 1 10	100				
Test for overall effect:	Z = 1.16	(P = 0.2)	25)				0.01 0	Case Control	100

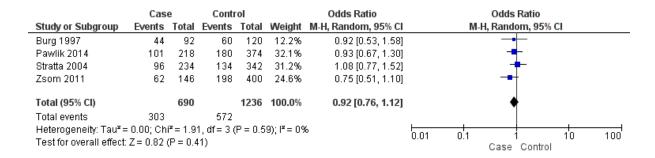
**Supplementary Figure S2h:** Forest plot - *ACE* I/D investigation, individuals with end-stage renal disease linked to type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a European population (*ACE* insertion compared to deletion).



**Supplementary Figure S2i:** Forest plot - *ACE* I/D investigation, individuals with IgA nephropathy compared to healthy controls in an East Asian population (*ACE* insertion compared to deletion).

	Case Control			ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Burg 1997	26	54	60	120	5.6%	0.93 [0.49, 1.77]	<del></del>
Drouet 2002	78	250	54	154	12.8%	0.84 [0.55, 1.29]	<del></del>
Harden 1995	79	200	76	196	14.3%	1.03 [0.69, 1.54]	+
Pawlik 2014	25	62	180	374	7.8%	0.73 [0.42, 1.26]	<del></del>
Pei 1997	145	336	91	200	18.7%	0.91 [0.64, 1.29]	<del>-</del>
Schmidt 1995 A	168	408	197	468	32.0%	0.96 [0.74, 1.26]	+
Stratta 1999	62	162	38	100	8.8%	1.01 [0.61, 1.69]	_
Total (95% CI)		1472		1612	100.0%	0.93 [0.80, 1.08]	•
Total events	583		696				
Heterogeneity: Tau² = Test for overall effect:				P = 0.9	6); I² = 09	6	0.01 0.1 1 10 100 Case Control

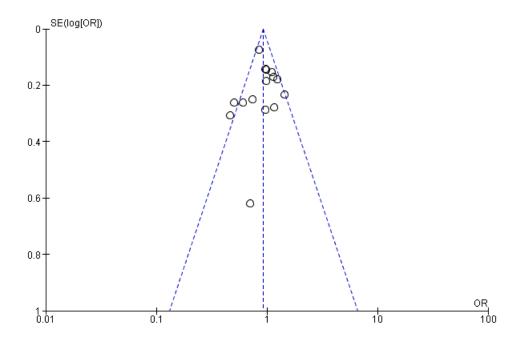
**Supplementary Figure S2j:** Forest plot - *ACE* I/D investigation, individuals with IgA nephropathy compared to healthy controls in a European population (*ACE* insertion compared to deletion).



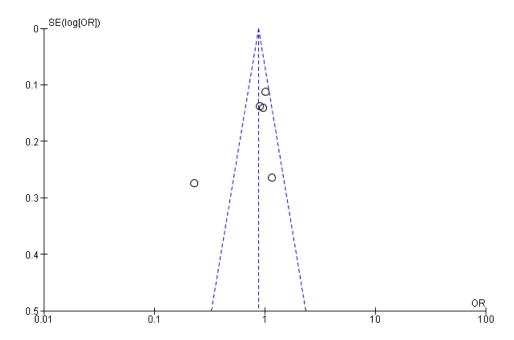
**Supplementary Figure S2k:** Forest plot - *ACE* I/D investigation, individuals with primary glomerulonephritis compared to healthy controls in a European population (*ACE* insertion compared to deletion).

	Cas	e	e Control			Odds Ratio		Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M	-H, Random, 95% (	3	
Beige 1997	251	538	244	538	27.2%	1.05 [0.83, 1.34]		+		
El-Essawy 2002	246	588	170	362	24.7%	0.81 [0.62, 1.06]				
Hueso 2004	122	360	96	226	18.2%	0.69 [0.49, 0.98]		-		
Stratta 2008	122	338	112	338	20.0%	1.14 [0.83, 1.57]		+		
Viklický 2001	28	60	599	1306	9.9%	1.03 [0.61, 1.73]		+		
Total (95% CI)		1884		2770	100.0%	0.93 [0.77, 1.11]		•		
Total events	769		1221							
Heterogeneity: Tau² =	0.02; Ch	$i^2 = 6.5$	9, df = 4 (	P = 0.1	6); I <sup>2</sup> = 39	1%	0.01 0.1	<del>-  </del>	10	100
Test for overall effect:	Z = 0.80	(P = 0.4)	12)				0.01 0.1	Case Control	10	100

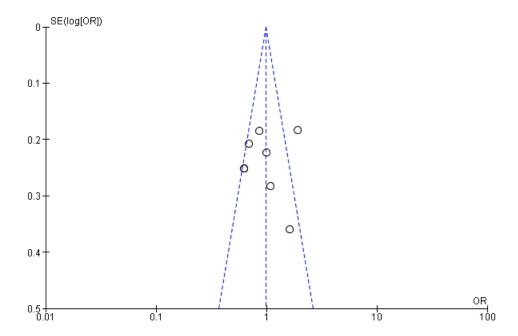
**Supplementary Figure S2I:** Forest plot - *ACE* I/D investigation, individuals who have had renal transplants compared to healthy controls in a European population (*ACE* insertion compared to deletion).



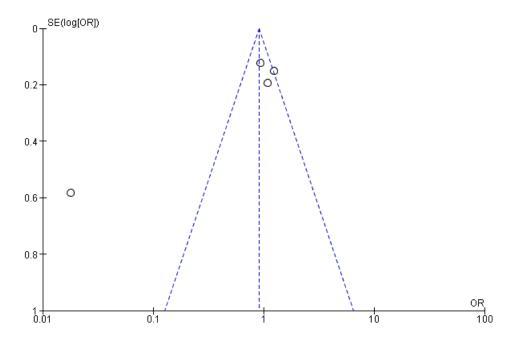
**Supplementary Figure S3a:** Funnel plot - *ACE* I/D investigation, individuals with type 1 diabetic nephropathy compared to individuals with type 1 diabetes mellitus in a European population (*ACE* insertion compared to deletion).



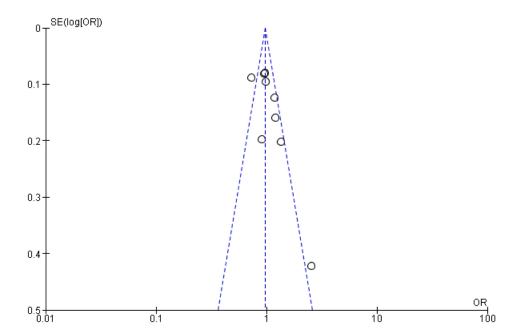
**Supplementary Figure S3b:** Funnel plot - *ACE* I/D investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a European population (*ACE* insertion compared to deletion).



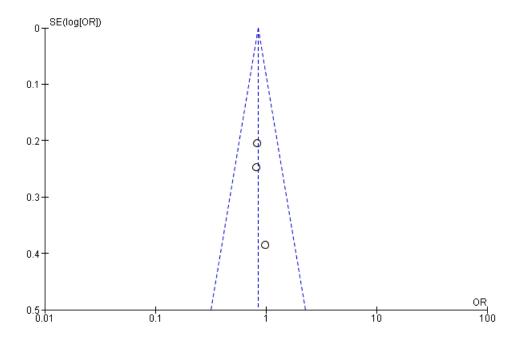
**Supplementary Figure S3c:** Funnel plot - *ACE* I/D investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a Middle Eastern population (*ACE* insertion compared to deletion).



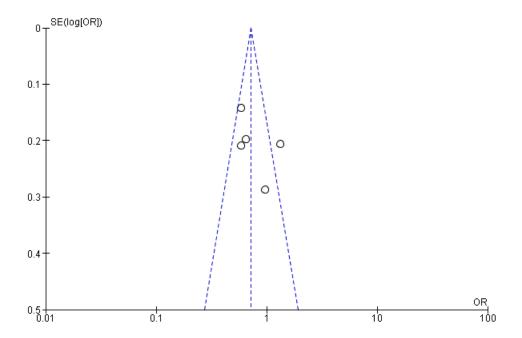
**Supplementary Figure S3d:** Funnel plot - *ACE* I/D investigation, individuals with chronic kidney disease compared to healthy controls in a South Asian population (*ACE* insertion compared to deletion).



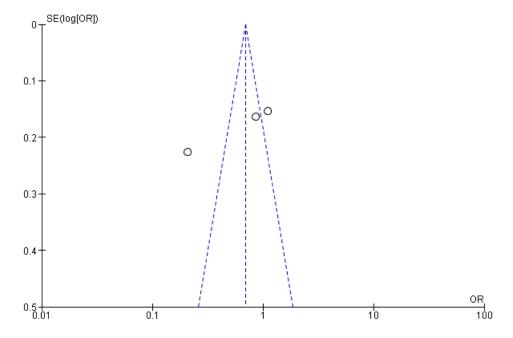
**Supplementary Figure S3e:** Funnel plot - *ACE* I/D investigation, individuals with end-stage renal disease compared to healthy controls in a European population (*ACE* insertion compared to deletion).



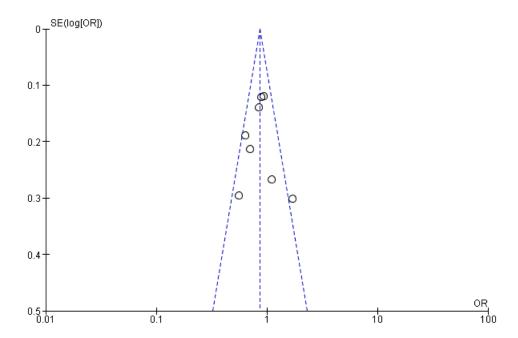
**Supplementary Figure S3f:** Funnel plot - *ACE* I/D investigation, individuals with end-stage renal disease compared to healthy controls in a Middle Eastern population (*ACE* insertion compared to deletion).



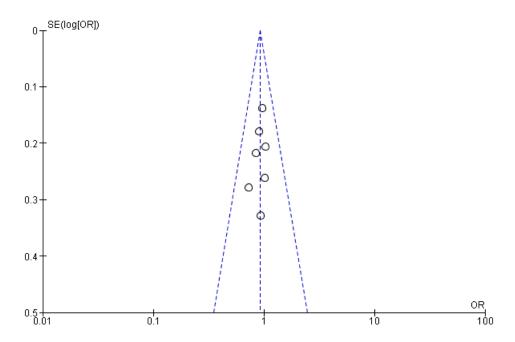
**Supplementary Figure S3g:** Funnel plot - *ACE* I/D investigation, individuals with end-stage renal disease linked to type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in an East Asian population (*ACE* insertion compared to deletion).



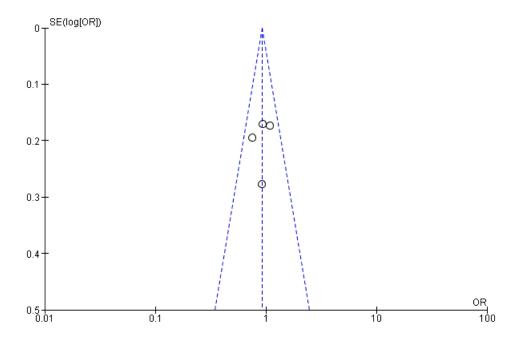
**Supplementary Figure S3h:** Funnel plot - *ACE* I/D investigation, individuals with end-stage renal disease linked to type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a European population (*ACE* insertion compared to deletion).



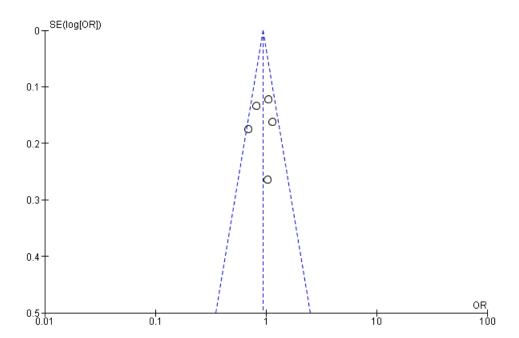
**Supplementary Figure S3i:** Funnel plot - *ACE* I/D investigation, individuals with IgA nephropathy compared to healthy controls in an East Asian population (*ACE* insertion compared to deletion).



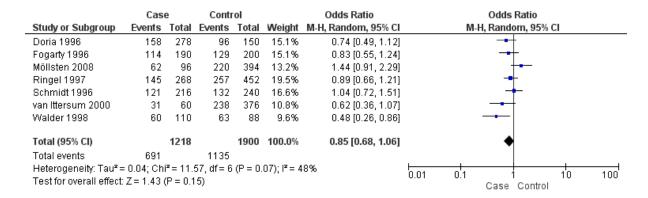
**Supplementary Figure S3j:** Funnel plot - *ACE* I/D investigation, individuals with IgA nephropathy compared to healthy controls in a European population (*ACE* insertion compared to deletion).



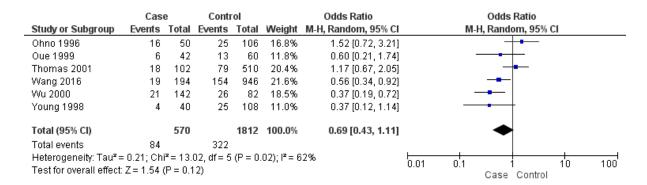
**Supplementary Figure S3k:** Funnel plot - *ACE* I/D investigation, individuals with primary glomerulonephritis compared to healthy controls in a European population (*ACE* insertion compared to deletion).



**Supplementary Figure S3I:** Funnel plot - *ACE* I/D investigation, individuals who have had renal transplants compared to healthy controls in a European population (*ACE* insertion compared to deletion).



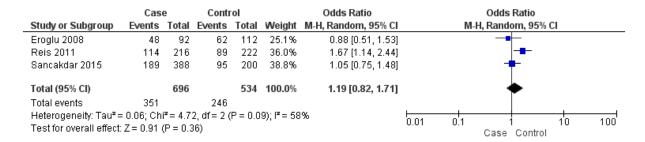
**Supplementary Figure S4a:** Forest plot - *AGT* rs699 investigation, individuals with type 1 diabetic nephropathy compared to individuals with type 1 diabetes mellitus in a European population (*AGT* rs699 T allele compared to C allele).



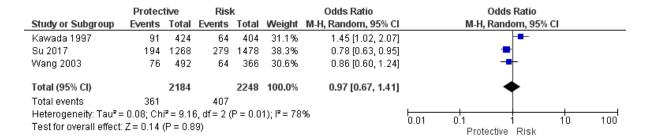
**Supplementary Figure S4b:** Forest plot - *AGT* rs699 investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in an East Asian population (*AGT* rs699 T allele compared to C allele).

	Cas	е	Conti	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	I M-H, Random, 95% CI
Fradin 2002	45	78	139	236	7.5%	0.95 [0.57, 1.60]	] —
Freire 1998	134	230	148	236	14.5%	0.83 [0.57, 1.20]	] <del> </del>
Makuc 2017	294	552	394	750	41.4%	1.03 [0.83, 1.28]	]
Schmidt 1996	149	254	117	214	14.9%	1.18 [0.81, 1.70]	] <del> -</del>
Zychma 2000	133	254	242	486	21.8%	1.11 [0.82, 1.50]	j <del>-</del>
Total (95% CI)		1368		1922	100.0%	1.03 [0.89, 1.18]	ı •
Total events	755		1040				
Heterogeneity: Tau² =	0.00; Ch	$i^2 = 2.1$	1, df = 4 (	P = 0.7	2); $I^2 = 09$	6	0.01 0.1 1 10 100
Test for overall effect:	Z = 0.39	(P = 0.7)	'0)				Case Control

**Supplementary Figure S4c:** Forest plot - *AGT* rs699 investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a European population (*AGT* rs699 T allele compared to C allele).



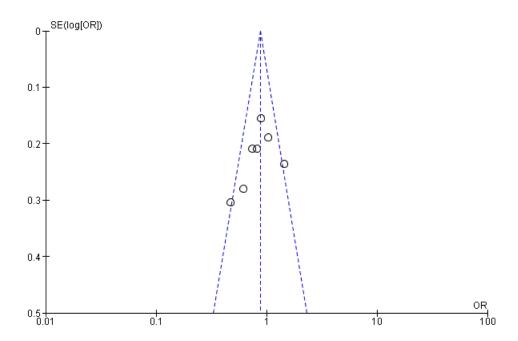
**Supplementary Figure S4d:** Forest plot - *AGT* rs699 investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a Middle Eastern population (*AGT* rs699 T allele compared to C allele).



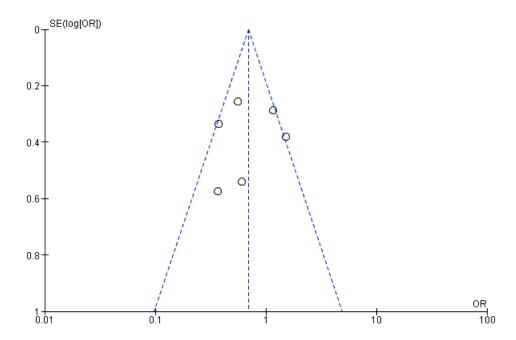
**Supplementary Figure S4e:** Forest plot - *AGT* rs699 investigation, individuals with end-stage renal disease compared to healthy controls in an East Asian population (*AGT* rs699 T allele compared to C allele).

	Case Control				Odds Ratio		Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	- 1	M-H, Random, 95%	i CI	
Gao 2015	144	700	125	620	41.2%	1.03 [0.78, 1.34]		+		
Guo 2016	19	90	16	90	5.4%	1.24 [0.59, 2.60]		<del></del>		
Huang 2010	35	260	40	240	12.3%	0.78 [0.48, 1.27]		<del></del> +		
Kim 2009	89	476	115	600	31.5%	0.97 [0.71, 1.32]		+		
Lau 2004	27	236	31	188	9.6%	0.65 [0.38, 1.14]				
Total (95% CI)		1762		1738	100.0%	0.94 [0.79, 1.12]		•		
Total events	314		327							
Heterogeneity: Tau² =	0.00; Ch	i² = 3.1	8, df = 4 (	P = 0.5	3); I² = 09	6	0.01 0.1		10	100
Test for overall effect:	(P = 0.6)	50)				0.01 0.1	Case Contro		100	

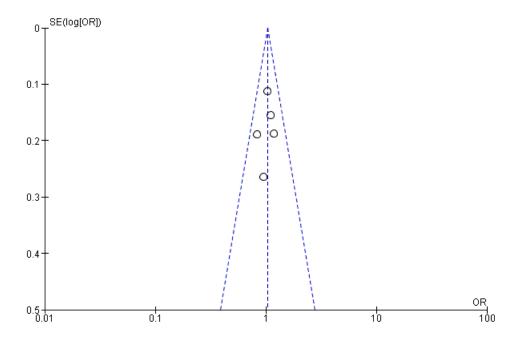
**Supplementary Figure S4f:** Forest plot - *AGT* rs699 investigation, individuals with IgA nephropathy compared to healthy controls in an East Asian population (*AGT* rs699 T allele compared to C allele).



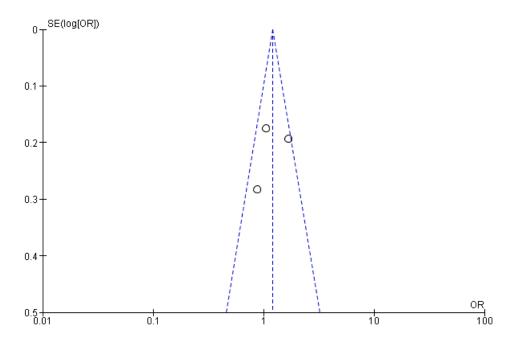
**Supplementary Figure S5a:** Funnel plot - *AGT* rs699 investigation, individuals with type 1 diabetic nephropathy compared to individuals with type 1 diabetes mellitus in a European population (*AGT* rs699 T allele compared to C allele).



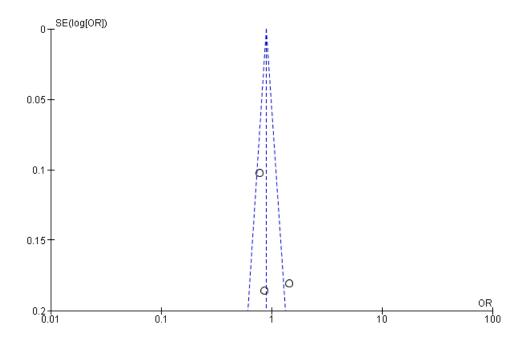
**Supplementary Figure S5b:** Funnel plot - *AGT* rs699 investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in an East Asian population (*AGT* rs699 T allele compared to C allele).



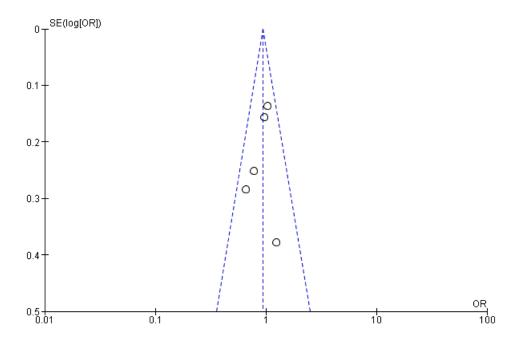
**Supplementary Figure S5c:** Funnel plot - *AGT* rs699 investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a European population (*AGT* rs699 T allele compared to C allele).



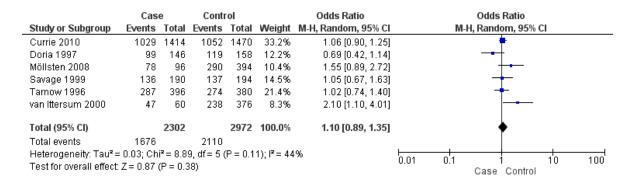
**Supplementary Figure S5d:** Funnel plot - *AGT* rs699 investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in a Middle Eastern population (*AGT* rs699 T allele compared to C allele).



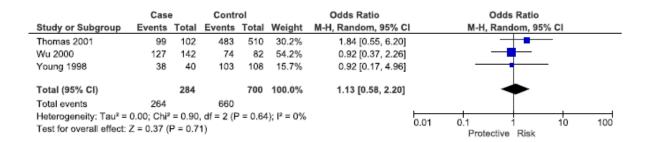
**Supplementary Figure S5e:** Funnel plot - *AGT* rs699 investigation, individuals with end-stage renal disease compared to healthy controls in an East Asian population (*AGT* rs699 T allele compared to C allele).



**Supplementary Figure S5f:** Funnel plot - *AGT* rs699 investigation, individuals with IgA nephropathy compared to healthy controls in an East Asian population (*AGT* rs699 T allele compared to C allele).



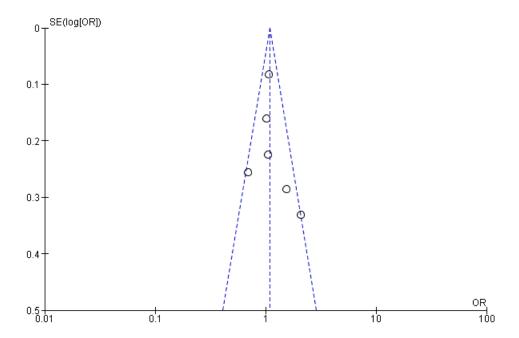
**Supplementary Figure S6a:** Forest plot - *AGTR1* rs5186 investigation, individuals with type 1 diabetic nephropathy compared to individuals with type 1 diabetes mellitus in a European population (*AGTR1* rs5186 A allele compared to C allele).



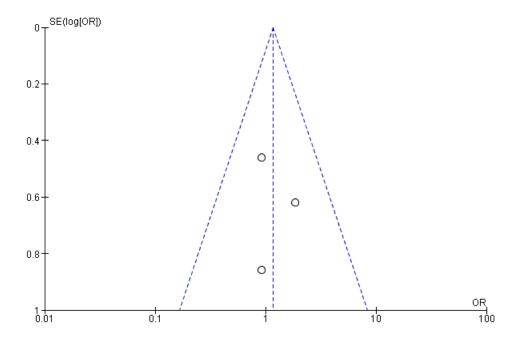
**Supplementary Figure S6b:** Forest plot - *AGTR1* rs5186 investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in an East Asian population (*AGTR1* rs5186 A allele compared to C allele).

	Case	9	Contr	ol		Odds Ratio		Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	l	M-H, Random, 95% CI	
Gao 2015	659	702	577	620	45.1%	1.14 [0.74, 1.77]		-	
Huang 2010	243	260	220	240	19.1%	1.30 [0.66, 2.54]		<del>- </del>	
Kim 2009	452	476	576	600	25.7%	0.78 [0.44, 1.40]		<del></del>	
Lau 2004	227	236	178	188	10.1%	1.42 [0.56, 3.56]		<del> -</del>	
Total (95% CI)		1674		1648	100.0%	1.09 [0.81, 1.46]		<b>*</b>	
Total events	1581		1551						
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup>	= 1.85	, df = 3 (F	0.60	); I <sup>2</sup> = 0%		0.01	0.1 1 10	100
Test for overall effect: 2	Z = 0.55 (	P = 0.5	8)				0.01	Protective Risk	100

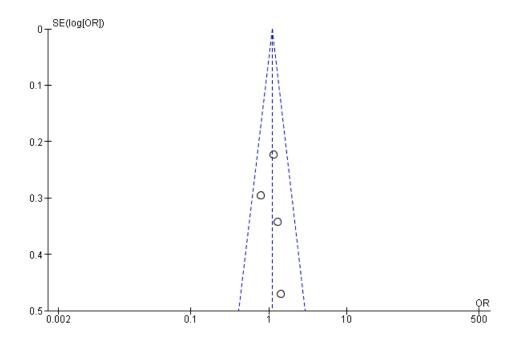
**Supplementary Figure S6c:** Forest plot - *AGTR1* rs5186 investigation, individuals with IgA nephropathy compared to healthy controls in an East Asian population (*AGTR1* rs5186 A allele compared to C allele).



**Supplementary Figure S7a:** Funnel plot - *AGTR1* rs5186 investigation, individuals with type 1 diabetic nephropathy compared to individuals with type 1 diabetes mellitus in a European population (*AGTR1* rs5186 A allele compared to C allele).



**Supplementary Figure S7b:** Funnel plot - *AGTR1* rs5186 investigation, individuals with type 2 diabetic nephropathy compared to individuals with type 2 diabetes mellitus in an East Asian population (*AGTR1* rs5186 A allele compared to C allele).



**Supplementary Figure S7c:** Funnel plot - *AGTR1* rs5186 investigation, individuals with IgA nephropathy compared to healthy controls in an East Asian population (*AGTR1* rs5186 A allele compared to C allele).